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REAL AND APPARENT DIFFERENCES

IN THE

INCIDENCE OF CANCER.

BY

E. F. BASHFORD, M.D.,

GENERAL SUPERINTENDENT OF RESEARCH AND DIRECTOR OF THE LABORATORIES,
IMPERIAL CANCER RESEARCH.

Reprinted from the TRANSACTIONS OF THE EPIDEMIOLOGICAL SOCIETY OF
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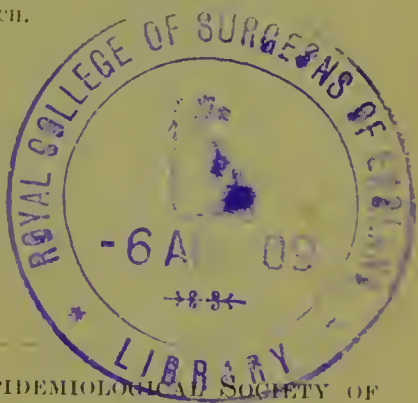
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INCIDENCE OF CANCER.¹

THE separation of the real from the apparent differences in the incidence of cancer is the immediate goal of the statistical study of malignant new growths. The separation is difficult to effect. In attempting to distinguish some apparent differences, and to emphasise others which appear to me to be real, I shall have to crave your indulgence. It will be necessary to discuss many topics not obviously associated and to endeavour to unravel a mass of detailed observations. Within the short space at my disposal, I shall require to be as dogmatic as possible, in order to bring out the differences which seem to be of real importance at the present time.

At the outset, therefore, I wish to guard myself against the imputation that I attach no importance whatsoever to many of the differences I shall describe as more apparent than real. I shall assign them to these respective categories with reference to their direct bearing upon experiment, in the present state of our knowledge.

The study of all the circumstances associated with the sporadic occurrence of cancer must remain indispensable so long as we are unable to test the relative importance of each. The relative importance of some of these circumstances can only be finally cleared up after the true nature of cancer has been ascertained, and the purely statistical investigation of the incidence of cancer will remain more or less empirical until this end is attained. The statistical investigation of infective diseases was pursued empirically before the developments of bacteriology directly demonstrated the causes of many of those diseases, and placed new problems before statisticians, who were enabled by those developments to see old problems in their true perspective, *e.g.*, the geographical distribution of infective

¹ The term "cancer" is used throughout for convenience to designate malignant new growths of all descriptions.

diseases, their epidemic and endemic occurrence, the relation between variations in the incidence of infective diseases, and, *e.g.*, water supply, density of population, rainfall, ground-water, or season. In the case of cancer, the statistical investigator has not yet advanced from the state of ignorance in which the student of the infective diseases compiled statistics in the days before Pasteur and Koch, and it would be unjust to criticise the uses accurate statisticians make of the available data.

Until we shall be able to start cancerous proliferation in a tissue at will, we shall remain in this same unfavourable position for determining the true importance of many circumstances, which at the same time it is unjustifiable to ignore. The increased number of deaths recorded from cancer, its apparent greater frequency in some geographical areas (whether large or small) than others, the presumable importance of race, diet, soil, climate, are all problems of much less importance than the infective or non-infective nature of cancer; but we must not lose sight of the fact that it is in all probability as much without the province of statistics to supply the direct answer to the question, What is the cause of cancer? as it was for statistics to directly prove the causes of diseases now known to depend on infective organisms.

Much harm has resulted from the improper use of statistics by those too enthusiastic advocates of this or that speculation on the nature of cancer, who have ignored the limitations to statistical investigations. Accurate statistics of all the circumstances associated with the sporadic appearance of cancer have their proper place. They are at present the best guide in defining the direction experimental investigation into the nature of cancer should take.

Statistics must be based on accurate data of a nature fitted to the end in view. In the case of cancer, there is a peculiar difficulty in securing accuracy in the data. There is lack of uniformity in the method of compiling existing statistics.

In a general survey of statistics on the incidence of cancer, variations in its recorded frequency are the outstanding feature. These variations have attracted much attention, but there is no unanimity as to the conclusions to be drawn from them.

Cancer is more frequently recorded in some countries and races of mankind than in others. Its recorded frequency varies in the same country, and in urban and rural districts at different times; and in more limited areas, *e.g.*,

in streets and houses, importance has even been attached to the larger number of cases of cancer treated in hospitals nowadays. As is well known, the frequency of cancer increases with advancing years, and it attacks the several organs of the body with varying frequency. The belief was at one time general that the disease was peculiar to mankind, but cancer is now known to occur throughout vertebrate animals. Here again its appearance presents irregularities, in that it is more common in domesticated animals than in wild animals, and more frequent in some domesticated animals than in others. A scrutiny of the nature of the data on which statements of this varying incidence are based is a necessary preliminary in order to arrive at provisional conclusions on the importance of each of the above-mentioned variations. Above all, it is essential to determine if any variable bears directly on the remaining variations, diminishing or augmenting their magnitude, or absolutely changing their significance.

DIFFICULTY OF RECOGNISING CANCER.

The pathological value of the data on which statistics of cancer are based is of prime importance. In the exanthemata and other infective diseases, the fully-developed disease, once it has been recognised as a clinical entity, presents itself in the mortality returns as a magnitude which can be compared from year to year, for there is a definite something to be recognised and recorded. Thus, for example, diphtheria, in addition to larval and ambulatory forms, occurs as a well-marked clinical entity in the majority of cases; so that its recognition nowadays presents fairly constant difficulties, and its relation to the general death-rate can be compared from year to year. The same may be said of tubercle, diabetes, and exophthalmic goitre. In cancer, on the contrary, we have to deal with the difficulty that the fully-developed disease, progressing to a fatal issue, may be entirely overlooked by the most competent observer, and not in a small proportion of cases, but even in so high a proportion as 50 per cent., *e.g.*, in the fatal internal cancers. Hence the records of deaths and estimates of mortality from cancer from clinical data alone, may vary within wide limits, the absolute incidence of the disease remaining, however, the same.

In order to obtain an estimate of the range of these limits, an attempt has been made to correlate the most reliable form of clinical diagnosis with the results of skilled

pathological examination in every case. This was achieved by the collaboration of members of the staffs of the large London hospitals providing succinct records of the cases of cancer in their practice, as well as of those cases which, although regarded clinically as malignant disease, were found on pathological examination not to be so. Thus the diagnosis of cancer was confirmed by pathological investigation in 3576 cases; 319 cases similarly diagnosed were found not to be malignant new growths at all, or nearly 10 per cent.; 726, or 16 per cent. of the cases in which diagnoses other than that of malignant new growth had been made, were discovered on pathological examination to be malignant new growths.

The importance of these figures for all statistical investigations of cancer is clearly manifest when the proportions of cases not diagnosed, and wrongly diagnosed, are studied according to the sites of the body in which the disease had originated. Those parts of the body easily accessible to complete physical examination are contrasted in the accompanying Table with inaccessible sites, and with sites intermediate between the two.

LONDON HOSPITALS.

Analysis of Cases Reported by the Hospital Authorities.

			Malignant New Growths.		
			Correctly Diagnosed.	Not Diagnosed.	Wrongly Diagnosed as Cancer.
Accessible	2391	218	190
Inaccessible	614	420	68
Intermediate	571	88	61
—			3576	726	319

The result appears conclusive as to the factor determining the accurate recognition of malignant new growths in hospitals. More than half of the cases not diagnosed (420 in 726) occur in inaccessible sites. While less than 10 per cent. of the malignant new growths in accessible sites are not diagnosed, more than 40 per cent. of those in inaccessible situations are clinically unrecognisable as cancer.

The pathological process is the same in all the different sites of the body. The great difficulty of diagnosing malignant new growths in internal organs is due to the

fortuitous and occasional character of the symptoms on which the diagnoses are based. Surgeons are more and more recognising that cachexia, pain, and other reputed symptoms are inconstant accompaniments of malignant new growths. Wilks¹ pointed out emphatically, forty years ago, as the result of experience gained in the performance of 2000 autopsies at Guy's Hospital, "the cachetic condition spoken of in cancer is a result of the disease, and does not pre-exist, and in very many cases is not present at all, and depends, as we have before remarked, upon accidental circumstances." The experimental study of cancer in animals fully justifies the conclusion Sir Samuel Wilks—the *doyen* of English pathologists—came to so long ago. The survival to the present day of this phantom symptom of cancer is but one illustration of the impossibility of setting up any better substitute or any series of signs as the characteristic symptoms of the disease. This impossibility, revealed by the figures quoted above, needs only one other illustration. Distinguished surgeons have confessed that they could not always be sure of the nature of certain morbid growths. They have got out of the difficulty by designating a group of conditions as pre-cancerous, because, although not conforming to the empirical symptomatology of cancer, cancer as a matter of fact frequently followed. To take the case of the tongue: here this state of affairs persisted till, with the valuable collaboration of Mr. Butlin, whose experience of such conditions of the tongue is perhaps unrivalled, Murray and myself were able to show that four out of seven lesions which Mr. Butlin believed to be pre-cancerous conditions of the tongue were in reality already well-developed, if small, epitheliomata and clinically unrecognisable as such. Here, in a site accessible to the most careful physical examination, the difficulty of diagnosis is clearly brought out. At the same time the probability of correct diagnosis is shown to depend not on symptoms, but on the size to which a cancer, a purely anatomical lesion, must attain before its character is recognisable to the unaided senses, or even with the assistance of the microscope.

The extent to which the difficulties of diagnosis tend to conceal the absolute incidence of cancer varies at different age-periods. The difficulties are more pronounced in children, for in them investigation is entirely objective, and the absence of features which are specific for cancer is most

¹ *Guy's Hospital Reports*, S. 111, vol. iv, 1868.

felt. A comparison of the percentage relationship of the distribution of malignant new growths (on the basis of the figures already quoted) at ages below 25, which were not diagnosed, and of those growths which had been wrongly diagnosed as cancer, brings out the fact that a much higher proportion of cases of malignant new growth cannot be recognised clinically in youthful patients. When the cases are grouped under ten instead of under twenty-five years, a still greater discrepancy is revealed.¹

We have no means at present of estimating the extent to which the figures of the cancer-mortality of the general population would be modified, were it possible to determine the disturbance introduced by cases wrongly diagnosed as cancer, and not diagnosed respectively. This difficulty is augmented by the fact that the figures, on which the estimate of the proportion of cases wrongly diagnosed as cancer is based, are derived from operation cases; while the estimate of the proportion of malignant new growths which were not recognised is based to a greater extent on post-mortem material, which compares much more strictly with mortality returns. In the national mortality returns the mode of death helps to decide whether the lethal issue was due to cancer or not.

It might seem that the errors in the final data, arising from the occurrence of growths wrongly diagnosed as cancer, will neutralise the under-estimate caused by cases which have not been diagnosed; but a little consideration shows that this is not the case. The under-estimate of the frequency of cancer is not uniform at all sites, and the sites where the under-estimate is greatest (internal organs) are not characterised by a corresponding over-estimate as the result of wrong diagnosis of cancer.

These considerations show that the errors in the one group cannot be set off against the opposite errors in the other group, in such a way that the final totals should represent the absolute incidence of the disease in any organ or in the body generally.

It is impossible to apply any correction from hospital statistics to general mortality statistics. It is therefore fallacious to make any direct comparison between the death-rates from cancer in the general population and the proportion of cases occurring in the patients of a hospital or group of hospitals, although the clinical observations which constitute the starting-point of both forms of statistics are

¹ Bashford and Murray, *The Statistical Investigation of Cancer, Sec. Sci. Rep. of Imp. Canc. Res. Fund* (Taylor and Francis, 1905).

similar. The death-rate of a population is the most—and probably the only—reliable method of estimating the frequency of cancer. All other methods, such as the German “cancer-census,” the study of the frequency in the experience of life-assurance societies, the comparison of the numbers of cases in hospital practice in which no basis for comparison exists, introduce either new sources of fallacy, or magnify those inherent in mortality statistics. The errors in diagnosis made in general practice are probably greater than in hospital practice, for they are made under less favourable circumstances.

In endeavouring to estimate the importance of the variations in the incidence of cancer, I shall attach great importance to the very wide limits within which the primary data may vary qualitatively and quantitatively under different circumstances.

APPARENT DIFFERENCES IN THE RECORDED INCIDENCE OF CANCER IN EUROPE.

There are differences in the number of deaths assigned to cancer in civilised countries. Owing to their exceptional characters, I do not propose to touch upon the statistics of the United States or of the Australasian Colonies. In Europe, *e.g.*, the rate of mortality varies from 0.33 in Hungary to 1.26 in Switzerland. It may not be only a coincidence that the largest number of deaths assigned to cancer occurs in Switzerland¹, where medical inspection of the dead body is customary, and where in 1900 in 15 of the largest towns autopsies were made in so high a proportion as 25.7 per cent. of the total deaths. I cannot refrain from pointing out that the number of deaths assigned to cancer increases from one country to another in a manner parallel with the increasing accuracy of the vital statistics of the several countries. Thus, for example, the Prussian statistics are known to be less reliable than those compiled by Dr. Tatham for England and Wales, and the rate of mortality from cancer is 0.57 as compared with 0.79. The recorded death-rate from cancer in Ireland is much smaller than in the rest of the United Kingdom, being 0.57, equal to that of Prussia; and I may take this difference as a special test case, because a possible explanation has been arrived at for Ireland.

The discrepancy between the recorded incidence of

¹ Cf., however, p. 11, for factors artificially augmenting the number of deaths from cancer.

cancer in England and Wales, and Ireland, exists also in the extent to which cancer is recorded in the hospitals of the two countries.¹ The fact has been elicited that autopsies are performed with minimal frequency in Irish hospitals,² whereas in English hospitals they add largely to the certified number of deaths from cancer. Further, in Ireland microscopical examination is scarcely carried out at all, outside of one or two centres of population; and in England, together with the number of autopsies, is responsible for adding over 30 per cent. to the total number of cases recorded in hospital.

A general review of the facts elicited on the diagnosis of cancer in London and Irish hospitals reveals the magnitude of the differences which may exist between the recorded frequency of cancer and its absolute incidence. Procedures, which in London and England generally make the recorded frequency approximate more nearly to the absolute incidence, are inoperative in Ireland. The discrepancy between the recorded frequency of cancer in London and Irish hospitals can be explained solely by the heavy disadvantage under which the search for cancer is carried out in the latter. The very unsatisfactory circumstances under which a large proportion of medical practitioners have to eke out an existence in Ireland is notorious, and finds its counterpart in the registration of the causes of death.

The conclusion is permissible that among that proportion of the Irish population which does not have access to hospitals, a still higher percentage of cases of cancer remains unrecorded; with the result that the relative frequency in hospital and the relative infrequency outside of hospitals, together combine to give a lesser-recorded cancer mortality throughout Ireland generally. In all probability, the more favourable conditions prevailing in England, if they existed in Ireland, would quickly demonstrate there a cancer death-rate proportionately higher than that of England, in accordance with the higher "age-constitution" of the Irish population.

The occurrence of cancer in Ireland has been made the subject of a special report by the Registrar-General for Ireland,³ the perusal of which only confirms the unfavour-

¹ Cf. Bashford and Murray, *The Statistical Investigation of Cancer*.

² Not only are the facilities for *post-mortem* examination lacking, but the habit of holding "wakes" on the dead is a great obstacle in the way of obtaining permission for autopsies.

³ "Special Report on Cancer in Ireland," Supplement to *Thirty-Eighth Annual Report of the Registrar General* (Dublin, 1903).

able opinion I have above expressed on the insufficiency and unreliability of the data upon which the Registrar-General of Ireland is obliged to rely for his statistics of cancer mortality; and also arouses misgivings as to the extent to which it has been found possible to apply actuarial corrections for the peculiar age-incidence of cancer.

Throughout Europe such disturbing factors are in play, minimising the number of the data available for statistical purposes in some instances, and augmenting them in others. The pathological value of the data is also by no means uniform. If one be justified in dismissing the difference between the rate of mortality in Ireland, and England and Wales, as an expression of an apparent and not of a real difference in the absolute incidence of cancer, the differences obtaining in the case of other European countries cannot have any greater importance attached to them. The primary data are obtained in different ways, and different statistical methods are employed in different countries. Therefore great caution is necessary in assuming that the final statistical results are comparable, and reveal real differences. In any case, the magnitude of the recorded differences loses much in significance. In some statistics, the attempt is made to deal separately with the deaths from sarcomata and carcinomata. This probably introduces grave errors, for Murray and myself have shown that the one form of disease is as difficult to recognise clinically as the other, and also that the probability is great that carcinoma and sarcoma both increase with advancing years: a conclusion to which Weinberg has come independently. In other statistics, new growths are grouped together, in a more indiscriminate fashion, *e.g.*, in Switzerland, for males, all fatal diseases of the prostate gland are grouped under the heading of "cancer" of that organ. The factor introducing most disturbance into the number and the value of the data is probably the manner in which the certification of deaths is effected, and the extent to which this is solely the duty of medical men, as in some States, or merely the ignorant opinion of a layman, after viewing the body, in others. Prinzing cites two instructive cases. In one, an ignorant peasant who performed this duty returned all deaths as due to cardiac failure, and another returned fifty deaths from diphtheria in Tilsit, at a time when even illness from diphtheria was quite rare.

The improvements Drs. Ogle and Tatham have effected in our own national statistics of cancer, by inquiring into vague statements of the cause of death, of itself serves to

show how much room there is for improvement in countries where laymen are entrusted with the declaration of the cause of death in the case of cancer—a disease often presenting insuperable difficulties to the most skilled clinician, as I have pointed out above with reference to hospitals.

Before the members of this Society it is unnecessary for me to emphasise that the statistical utilisation of the number of deaths recorded from cancer requires the employment of special methods, because of the frequency of the disease in old people and its rarity in the young. This fact has not received so much attention abroad as in England, where Newsholme has so ably enforced its statistical importance. I am obliged to draw attention to the frequency with which statistics on cancer have been compiled without any cognisance being taken (1) of the pathological value of the data; (2) of the actuarial corrections for the error due to the survival of a varying number of persons to higher ages; (3) of the futility of conclusions based on too small numbers, *e.g.*, in small districts. These are sources of fallacy any one of which may completely vitiate comparisons, and which, I regret to say, are not always absent from the reports of medical officers of health in this country, who occasionally alarm their neighbourhoods by, *e.g.*, permitting such statements as, "There was a considerable increase last year in the number of deaths from cancer, and also from whooping-cough and suicide."

In briefly summarising the impression made by a study of the death-rates from cancer in European countries, I may state that comparisons between different countries, with a view to establishing differences in the absolute incidence of cancer, appear to me to be entirely fallacious. The dimensions of the differences are not so great that they are incapable of explanation by (1) the varying difficulties in the way of obtaining accurate records of the numbers of deaths from the disease, *i.e.*, of making them approximate to the absolute number; (2) the divergences in the methods of utilising the data for statistics; (3) the varying extent to which actuarial correction is made for the age-constitutions of the respective populations; (4) the different age-constitutions of the populations themselves. I must guard myself from the charge that I deny real differences may exist. All I intend to convey is that the recognisable sources of fallacy appear to me to carry more weight than the evidence that the existing differences are real, and of sufficient magnitude to make them of primordial importance for the experimental investigation of the nature of

cancer. As regards more limited areas in single countries, and differences between towns and country districts, the accuracy of the registration of the causes of death is everywhere behindhand in rural districts as compared with towns; and the same remarks appear to be applicable here as to the differences which obtain in the rate of mortality from cancer in more extended areas.

APPARENT DIFFERENCES IN THE INCIDENCE OF CANCER OUTSIDE EUROPE.

When attention is directed to races of mankind outside of Europe, including aboriginal races, the differences in the recorded incidence of cancer are of greater magnitude. These differences are chiefly relied on by those who assert that our European civilisation is causally connected with the recorded increase in the number of deaths from cancer.

The case of Japan is of special interest. In 1901, the German Cancer Committee seriously accepted information to the effect that cancer was, without doubt, much rarer in Japan than in Europe. The informant went on to state: "This is at once evident from the relatively large number of cases in the small number of European inhabitants, as contrasted with the rarity with which the disease is observed in natives."¹ Without referring to the statistical fallacies which vitiate such a conclusion, it is sufficient to point out that, as a matter of fact, the official statistics of the Japanese Empire for that same year show that out of a total of 959,126 deaths, 24,598 were returned as due to "cancer" and "other malignant growths."²

I have to thank Baron Takaki for access to the Japanese statistics. He expressed the opinion that cancer was not so well diagnosed in Japan as in England, nor were the mortality statistics of Japan as yet comparable in accuracy to those of this country. The approximation of the Japanese to the English national figures is thus made all the more striking. The crude figures would indicate that cancer is twice as frequent as a cause of death in England as in Japan. It must be evident, without further discussion, that this conclusion might require drastic revision if our information as to the "age-constitution" of the Japanese population were more complete, and if the registration of

¹ *Verhandl. d. Comites f. Krebsforsch.*, Heft. 1, p. 46.

² In England and Wales in 1904, out of 549,784 deaths, 29,682 were returned as due to cancer. The population in 1904 was calculated to be 33,861,210. The population of Japan in 1901 was 45,227,464.

deaths were carried out as in this country. In Japan, in 1901, no fewer than 52,786 deaths were recorded as due to old age, and 113,474 as due to undefined diseases.

Exaggerated importance, not justified by fuller knowledge, has been attached to assertions that cancer is practically absent in India, in Egypt, and among aboriginal races.

In the course of the past two years 1288 cases have been reported from hospitals in India. Considering the 200,000,000 of population this number seems vanishingly small, but must be regarded in the light of the small number of hospitals, and the onerous duties which a relatively small number of officials, undertaking this additional work, have to discharge. More than 90 per cent. of the cases are recorded for sites very accessible to physical examination. The patients belong to vegetarian as well as other castes, and their distribution throughout India suffices to dispel any hopes of discovering races exempt from the disease in that country. The rarity in the records of cases from internal organs does not necessarily imply that such cases do not occur. The difficulty of diagnosing internal cancer has already been referred to as of statistical importance; and these difficulties must be much greater in circumstances such as are met with in India, and to a still higher degree in less civilised countries. In the case of Egypt, among the patients treated in the Government Hospitals, 193 cases of cancer have been reported during the past two years. In short, wherever there is a well organised medical service controlling hospitals in outlying parts of the empire, reports of the occurrence of cancer have been obtained, with certain exceptions where the smallness of the populations has precluded its occurrence up to date. The relative ease with which reports have been obtained through the instrumentality of the Colonial Office contrasts favourably with the difficulties to be overcome in obtaining the data.

I do not propose to discuss in detail the observations which have accumulated since the commencement of our inquiries, as to the occurrence of cancer in the native races in outlying parts of the British Empire and remote from civilisation. It will suffice to point out that the disease has been found where formerly it was supposed to be absent, but the figures are still too small to merit detailed consideration. The facts ascertained show that, taking England as a standard, there is a gradual diminution in

the precision and completeness with which cancer is recorded, Ireland showing less precision and completeness, and various outlying parts of the empire still less of these qualities, till a minimum is reached among the natives of certain tropical colonies, and in the case of islands with very small populations. The diminution proceeds *pari passu* with the increasing difficulties in observing the disease, or obtaining reliable primary statistical data of any sort whatsoever. These considerations modify the importance to be attached to differences in the recorded incidence of cancer in Japan, India, Egypt, and uncivilised races, for they are paralleled in Europe if in lesser degree.

It may be opportune to remark here that although cancer is universal, it is everywhere a rare disease. Even in countries in which it is a relatively important cause of death, the number of cases of illness from cancer is small in comparison with the total population. The differences in European countries only amount to fractional parts of 1 death per 1000 living. The data which would enable us to compare Central African with European races in the same way are totally wanting.

Reviewing the incidence as a whole, the balance of probability is in favour of the view that the recorded differences in the frequency of cancer in European and other races are more apparent than real. They are therefore unlikely to afford safe guidance to experimental investigations, or to throw direct light on the truth of the assumption they have so frequently been used to support, viz., that cancer is a disease, of which the several cases occurring in a population are causally connected by a common virus passed from one person, directly or indirectly, to another. I do not underrate the value of the statistical investigations above described, when I assert that their continuance does not promise to yield data numerous and reliable enough to reveal the real differences which may exist within a measurable time. Data bearing only on the ethnological distribution of the disease require to be supplemented by other investigations when we attempt to draw conclusions forthwith.

COMPARATIVE BIOLOGICAL IMPORTANCE OF THE AGE- INCIDENCE OF CANCER.

Throughout the ethnological distribution of cancer, one fact is constant and prominent. The maxima in the number of cases recorded always refer to later adult life or

advanced age. Progressive diminution in the recorded frequency of cancer, as described above, for the *genus homo* presents itself when consideration is turned to other representatives of the vertebrate phylum, and the frequency of cancer in domesticated and in wild animals is compared. If it be unjustifiable to directly compare the data on the incidence of cancer in different races of mankind, it is still less justifiable to compare the incidence of cancer in one class of the vertebrates with its incidence in others. Nevertheless, the data exhibit features which have important bearings upon the nature of cancer in man, even in the absence of valid statistical comparisons. In a series of papers, the importance has been emphasised of the occurrence of cancer in domesticated and in wild animals, and I must refer to them for details.

Investigation has proved that cancer occurs in mammals, tame and wild; in birds, tame and wild; in amphibia, in fresh-water and in marine fish, and its occurrence in the latter when living in a state of nature possesses no little interest. The only class of the vertebrates in which the disease has not been described is the reptiles, in whom, however, benign new growths are known to occur. In the case of some domesticated animals, *e.g.*, mice and cattle, the systematic examination of large numbers of animals has already shown that the frequency of the disease in them varies from one case in 1500 to one case in 3500, approximating therefore to the frequency of the disease in a population of all ages. Attention has only recently been directed to this matter. The data already obtained, however, appear to indicate that when the full facts are known, the frequency of cancer, at any rate in some domesticated mammals, will approximate very closely to that of civilised man. The most important result of this line of investigation is the establishment of the fact that the peculiar age-incidence of cancer in man is a law certainly for all the domesticated mammals. In the sparser data from other vertebrates, there is no evidence against its wider application; but, on the contrary, much that supports the view that cancer develops in constant relation to the absolute duration of life, whether it be long or short. At every step one has been met by the fact that the case with which cancer was discovered stood in direct relation to the number of aged animals examined, and to the extent of the facilities for making observations on them.

While new growths are less frequent in animals than in man, a consideration of the causes of this infrequency

serves only to emphasise the importance of old age in determining their occurrence. The relative infrequency with which new growths are recorded in animals other than man is probably due to various causes. Where the tenure of life is short, the period of comparative immunity from cancer is correspondingly shortened, but the period of maximum liability is still more greatly abbreviated; *e.g.*, in the case of the mouse, these periods are respectively two years and one year. In cases in which life is much longer than in man, *e.g.*, in many of the reptilia, where the duration of life is reckoned sometimes by hundreds of years, the total numbers of animals coming under observation at the time when they are most liable to cancer is extremely small. In the case of wild animals, those approaching decrepitude are either killed off or die of starvation. Under their natural conditions of life, animals rarely survive the period of functional activity of the reproductive organs. The cogency of these observations is reinforced by the relatively greater frequency with which cancer occurs in the domesticated mammals, and more particularly in those which, for sentimental or commercial reasons, are allowed to attain old age in relatively greater numbers, *e.g.*, in the horse, the dog, the cat, and old female cattle, where the latter are allowed to attain almost the absolute limit of life when peasants keep them for draught purposes, or for breeding. On the contrary, among those domesticated animals which are killed off when still young, so soon as they have become marketable commodities, *e.g.*, pigs, cancer is extremely rare. The frequency of cancer among the negroes of America contrasts with the difficulties encountered in searching for the disease among the natives in Central Africa; but it also adds force to the same line of argument. All the preceding considerations lead one to suspect that civilised man's responsibility for the occurrence of cancer among native races brought into contact with civilisation, and in domesticated mammals, may merely be limited to providing them with opportunities for reaching their respective cancer ages.

The comparative biological study of cancer has given new significance to the difference in the incidence of the disease in young and adult individuals. It is a real difference, and of fundamental importance in elucidating the nature of the disease. Accurate statisticians have long given careful attention to its statistical importance; and although it has been the stumbling-block of most hypotheses, pathologists in the past have not accorded it the importance it now deserves in the light of recent research.

The increasing frequency of malignant new growths as age advances in domesticated animals, and their restriction to advanced age in those animals in which only isolated cases have been observed, gives a totally different aspect to the age-incidence of cancer in man, the species in which our knowledge is most complete.

It has, indeed, been asserted repeatedly in Germany that cancer is becoming more frequent in young people than it was, and that the alleged increase of cancer is due partly to this phenomenon. The allegation of this departure from a biological law of such wide application as the age-incidence of cancer at once demands attention. The national mortality returns do not support this view for England and Wales, the increase in the recorded number of deaths being greater for the higher-age periods. As regards German statistics themselves, the figures for the town of Berlin indeed show exactly the opposite, a much greater apparent increase in higher ages. With reference to the Prussian statistics, Weinberg remarks: "In Prussia especially, mortality statistics have markedly improved, in so far as many towns have introduced death-certification by medical men, and in addition the populations of the towns have increased relatively and absolutely, side by side with the more accurate statistics pertaining to them. It is therefore not to be wondered at that Wutzdorff has recorded an increased frequency of cancer in the younger age-groups."¹

In asserting the fundamental importance of the increasing frequency of cancer with advancing years, one is at once confronted with the fact that cancer is not absent from early life,² but on the contrary occurs in measurable amount from birth onwards. The fact does not detract from the importance of its predominating association with senescence, for the organs attacked in the young acquire added interest, when once it is realised that the association of cancer with senescence may be of importance in framing conceptions of the nature of cancer, its conditions of origin, and the relations of cancerous proliferation to the growth of the individual.

¹ *Münch. Med. Woch.*, No. 50, 1905.

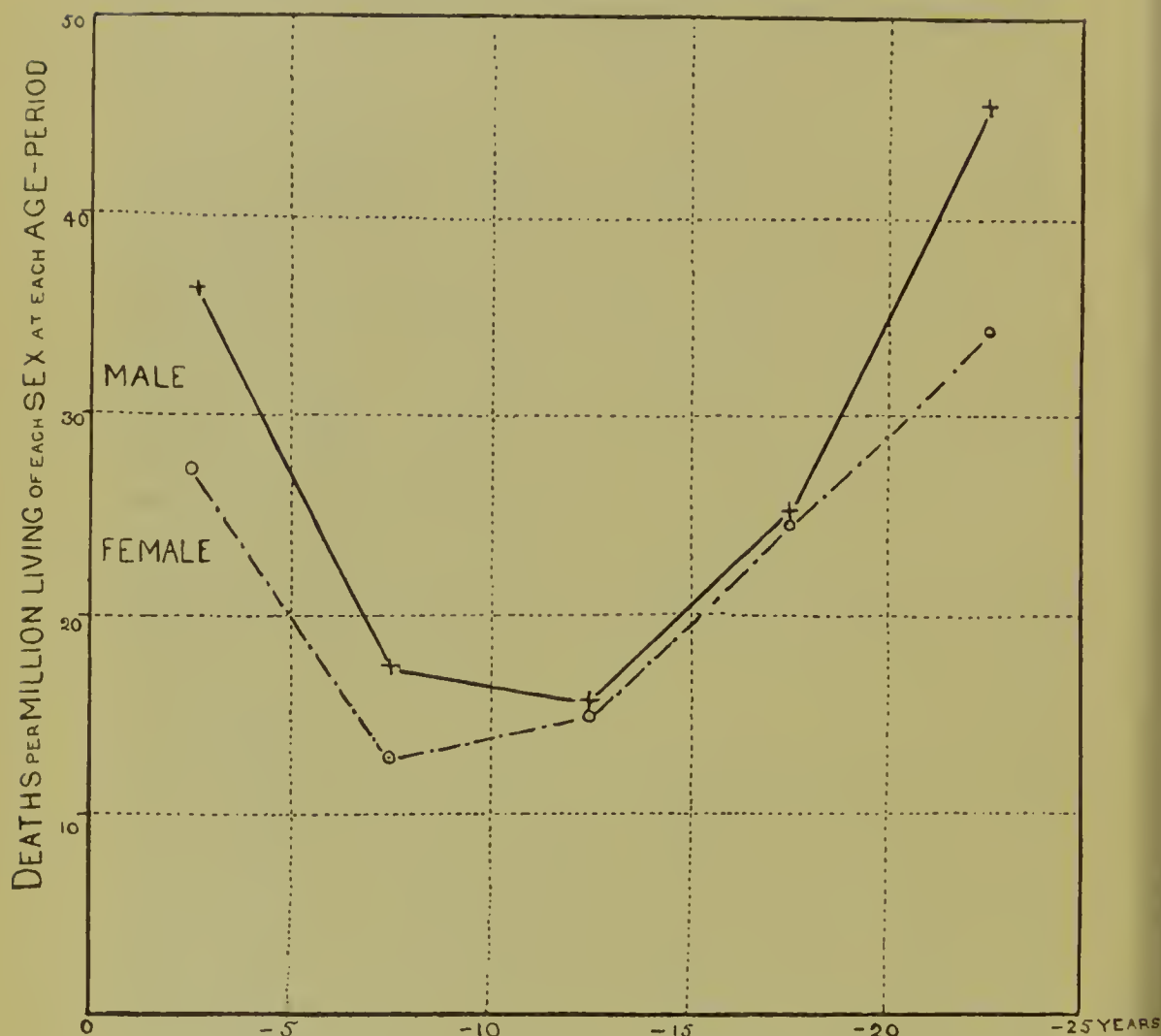
² In the same way a certain proportion of individuals reach extreme old age (90 years and over) without developing malignant new growths. Whether in these cases the period of liability has passed, and a condition attained comparable to the minimum in early life described below, or these aged people escape because of the absolute rarity of cancer even in the aged, cannot be determined at present with the data at my disposal.

The organ-incidence of cancer in children is apparently widely different from that which in later life makes up the great mass of fatal cases. Tumours of congenital origin—often of complicated structure—form a considerable proportion. Growths in the neighbourhood of the kidney, many of which probably fall into the same category, are also present in a considerable proportion of children dying of malignant disease. Sarcomata in various regions of the body, but especially in connection with the bones and the central nervous system, form a large contingent. The structures which in later life are especially prone to cancerous transformation are at this time almost entirely exempt. The years immediately following birth may be considered as a period of senescence of many foetal structures whose function has been fulfilled, and probably of many other formations which, although never exercising any function, and regarded as abnormalities and deformities, are yet merely pathological aberrations of structures normally present in man, or in lower animals. That many of the cancers met with in the earliest years of life may be special manifestations of the age-incidence of the disease is made possible by a peculiarity in the incidence of cancer at that period. When the death-rates from cancer in the general population of England and Wales at different age-periods are compared, the death-rate progressively diminishes as younger age-periods come under review. When the deaths from cancer of persons under twenty-five are stated as death-rates per million living at intervals of five years, it is found that the diminution does not extend uniformly back till birth. On the contrary, a minimum is reached between the fifth and fifteenth years. The mortality among females is also noticeably less than in males, in contrast to what obtains in later life. In the crude figures from hospitals the same features are present. This diminution in the cancer death-rate is sufficiently important to deserve attention. The statistics of mortality for Berlin, for Prussia, and for Bavaria exhibit the same minimum—also lower in females. It is the only minimum which the collective death-rate from cancer shows after birth, and appears to be an expression of a real difference in the incidence of the disease.

We can thus infer that it will be possible to attain to a further insight into the incidence of cancer when an analysis is made, not with reference to individuals, but with reference to the organs composing the body. The increase is not uniformly progressive and simultaneous for

all organs. The span of life of the individual is not the same as that of the separate organs and tissues contributing to its maintenance. The varying age-incidence of cancer in different organs of individuals of the human race presents contrasts similar to those found in different animals with long and short lives.

Cancer of the stomach becomes frequent earlier than



Death-Rates from Cancer in Persons of each Sex under 25 Years, at Five Age-Periods. Average for 1901. England and Wales.

cancer of the skin, cancer of the uterus and mamma are more frequent towards the decline of reproductive activity than in the earlier years of life; and, to take an extreme case, cancer of the chorion follows closely upon the period when this tissue, having fulfilled its transitory function, begins to undergo involution.¹

¹ For this reason ordinary chorion-epithelioma occurs fairly uniformly throughout the period of reproductive activity. The period of its greatest

Looked at biologically, chorion-epithelioma presents a perfect parallel in man to the incidence of cancer in short-lived animals.

Regarded from this standpoint, the age at which cancer is at a maximum in a population depends upon the ageing of the tissues in which it takes origin, much more than on the absolute ages of the individuals in whom it occurs. The sharp contrast prominent between long- and short-lived animals respectively is obscured for the organs of individuals. Just as two years old in one species of animal may correspond to sixty years old in another, so relatively wide limits obtain in the period within which the same tissues in different individuals enter upon their period of senescence. The future combination of statistical and other forms of study must determine whether anything comparable with the fall described for childhood occurs for individual tissues, *i.e.*, whether the individual tissues having passed a stage at which a maximum incidence is reached, the danger tends to diminish. The data at present available appear to indicate a progressive advance for some tissues, and a rise followed by a fall for other organs; but no definite conclusions may yet be drawn.¹

In the preceding pages I have attempted to show that the variations in the incidence of cancer in civilised peoples are not great, and are probably apparent. The nature of the evidence available with reference to the occurrence of cancer in uncivilised peoples and savage races has been reviewed. Here also the prominent differences obscure those that may be real.

All the obvious differences together have less value for investigation than one phenomenon which is of practically universal occurrence. The differences due to the relative proportion of aged individuals in a population, whether human or animal, are more constant and therefore real. They call urgently for explanation, and must engage the energies of those carrying on the study of cancer until solved. They are paralleled by the differences between the frequency of cancer in different organs of the human body in the English national statistics. They are directly accessible to statistical study, are real, and their accurate investigation has a direct bearing on the nature and

frequency must be considered biologically with reference to the generation of which it forms a part, *viz.*, the foetus and not the mother. It is, however, impossible to obtain this separation for statistical purposes.

¹ Many *aged* people escape the risk of cancer; cf. the remarks in footnote on p. 18.

ENGLAND AND WALES.

Deaths per 1,000,000 Living at each of the Age-Periods given. Average 1901 to 1904, illustrating the Different Age-Periods at which Cancer of Certain Organs begins to increase rapidly in frequency.

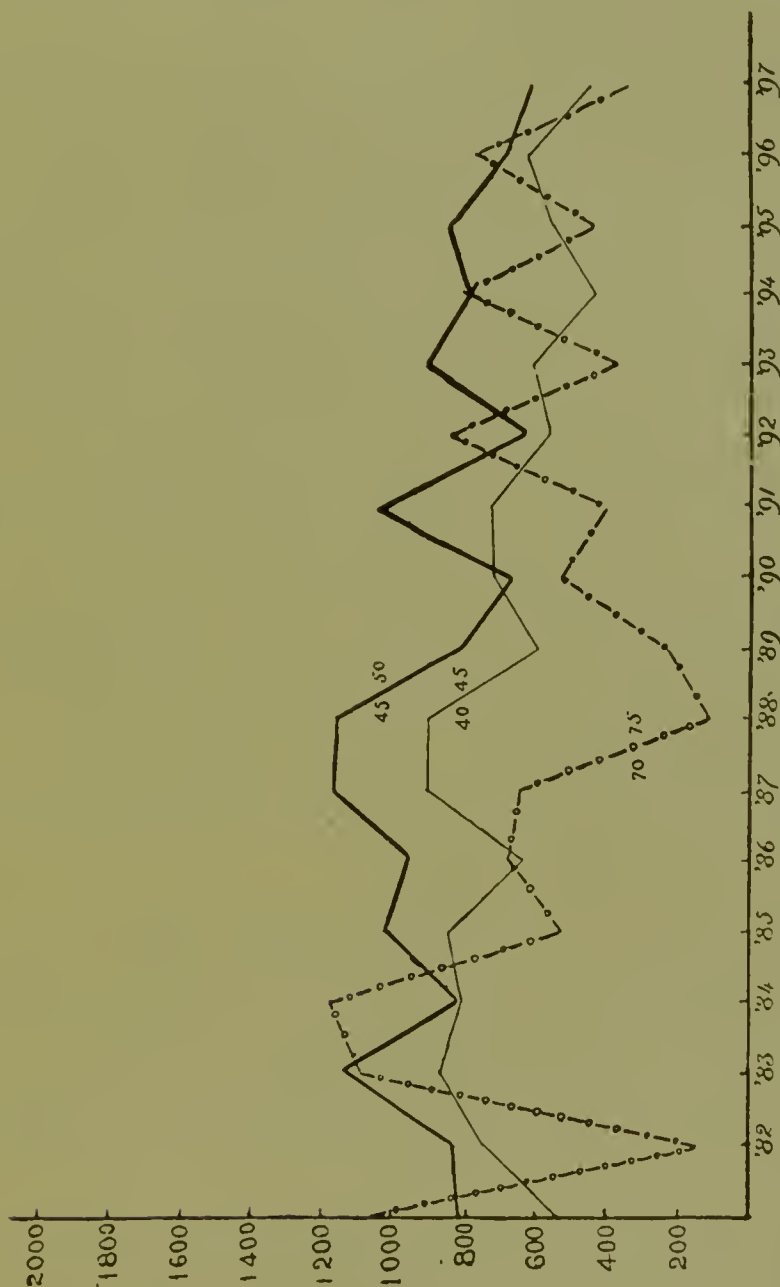
MALES.

	Under 5.	5 to 10.	10 to 15.	15 to 20.	20 to 25.	25 to 35.	35 to 45.	45 to 55.	55 to 65.	65 to 75.	75 to 85.	85 and upwards.
Skin ...	0.79	0.28	0.46	0.61	1.00	2.37	10.53	36.34	103.39	278.49	734.23	1650.20
Stomach	0.15	2.33	15.08	89.69	325.62	875.64	1530.94	1490.71	736.45
Rectum ...	0.13	...	0.46	0.91	4.83	10.94	35.90	142.54	393.57	718.54	826.19	668.26
Tongue	0.15	...	1.58	21.82	114.10	224.59	278.73	305.56	1772.94
Brain ...	3.30	3.38	2.49	2.90	3.33	6.31	10.66	16.50	20.25	13.34	2.97	—
Shoulder ...	0.26	0.14	0.29	0.61	0.83	0.89	1.01	2.11	4.05	8.72	14.83	13.64
Kidney and Adrenal	7.93	1.69	0.73	0.46	1.17	1.77	5.71	16.68	33.47	45.65	54.88	13.64

FEMALES.

Skin ...	0.53	0.14	0.15	0.15	0.30	1.06	4.39	15.29	32.65	97.87	267.48	553.62
Stomach ...	0.13	...	0.15	0.15	1.04	12.38	79.27	278.78	678.29	1195.33	1255.77	834.43
Rectum	1.49	2.23	11.05	36.31	122.80	271.13	441.41	552.15	312.91
Uterus ...	0.26	0.45	3.30	61.99	337.25	746.34	967.16	1012.29	910.94	730.13
Breast	0.15	0.15	0.74	20.16	168.86	460.28	699.11	966.42	1407.23	3013.88
Tongue ...	0.13	0.15	2.21	3.68	7.64	17.98	42.18	49.41	24.07
Brain ...	1.32	2.10	1.76	1.64	2.97	4.33	9.85	11.55	13.49	10.65	6.45	—
Shoulder	0.28	0.29	0.45	0.30	0.71	0.95	1.30	4.02	4.91	7.52	8.02
Kidney and Adrenal	8.16	1.54	0.59	0.60	0.59	1.33	5.70	16.92	28.39	43.41	54.79	24.07

incidence of cancer. The suggestion is made that the senescence of individual tissues plays an important *rôle* in determining the initiation of cancerous proliferation in those tissues, and indicates a line of inquiry, at once biological and statistical, which promises the most valuable results.



Cancer of Uterus : Berlin, Deaths per 1,000,000 at Three Quinquennial Age-Periods, from 1881 to 1897. (Extracted from data supplied by the late Professor Hirschberg, Director of the Statistical Bureau, Berlin.)

We may attempt to elucidate cancer on the basis that the disease arises *de novo* in each sporadic case, in conformity with a law according to which cancer is a "function of senescence" dependent on circumstances innate in each species of animal, and on the laws peculiar

to and controlling the growth and length of life of organisms as a whole, and of their individual organs. We may attempt to establish the existence of a common causal infective agent which is peculiar by being subject to the same law. Statistical and experimental study has thus far only yielded evidence in favour of purely biological, as opposed to bacteriological, conceptions of the nature of cancer.

I hope the general statements I have made will be accepted as evidence that the investigation of the circumstances associated with the sporadic appearance of cancer, and the manner of the appearance of the disease in individuals, are together still capable of maintaining alive interest in statistics of cancer, and even of directing them into new channels. The value of statistical inquiries rests on the control they afford of the conclusions derived from experimental investigations, and on the indications they give of the most favourable points of attack, they are indispensable to the correct formulation of the problems requiring experimental solution. I cannot do better than conclude by expressing thanks to Dr. Tatham for the willingness with which he has placed the resources of the General Register Office at the service of the Imperial Cancer Research Fund, with a view to promoting this end. The collaboration of a national statistical office has not been vouchsafed to the same extent to similar inquiries out of England, and I trust that this collaboration may materially contribute to extracting the essential problem from the surrounding obscurity.

DISCUSSION ON DR. BASHFORD'S PAPER.

THE PRESIDENT: I should like to say that since the establishment of the Imperial Cancer Research Fund I have been connected with the Committee of that Fund, and in that capacity I have been brought (very fortunately for me) into very frequent relation with my friend Dr. Bashford.

I think that I shall be expressing the sentiments of the majority of my colleagues in this Society if I say that we are impatient (perhaps too much so) to learn, on the one hand, what new light Dr. Bashford's painstaking researches can throw on the nature and cause of cancer; and, on the other hand, whether to-day we are any nearer than formerly to the discovery of a cure for cancer.

To take the last point first, Dr. Bashford tells us that, as

regards cure, the consequences he has described of inoculating a mouse with a mite of tissue no larger than a pin's point show how rational is the modern surgical treatment of the disease. He points to the fact that the early surgical removal of the small piece of tissue at the site of inoculation prevents the diffusion of the disease, and the formation of secondary deposits in remote parts of the body. This evidence, in his opinion, demonstrates the necessity for prompt removal of the smallest growths, as is now constantly advocated by surgeons, and too often as constantly neglected by patients.

In consequence of the difficulty of recognising cancer in its earliest stages, Dr. Bashford sees little hope that within a reasonable time primary growths will be amenable to anything short of absolute removal. On the other hand, however, he says that from the fact that animals can be rendered unsuitable for the growth in their bodies of malignant processes, we are entitled to hope that eventually we may be able to so far enhance the power of resistance of the organism that the cells disseminated from the site of inoculation shall be unable to grow.

As regards the nature of cancer, Dr. Bashford assures us with confidence that much more is now known than was the case a few years ago. At all events, the way has been cleared by the demolition of theories of causation, which were rife only very recently. The manner in which carcinoma can be transmitted from individual to individual has now been so fully established experimentally as to be no longer in doubt. The experimental transfer of the disease presents a striking contrast in this respect—that transference can be effected very much more readily to young than to old animals. This is in absolute contradiction to what might have been—and, as a matter of fact, was—expected. This difference between young and old animals is, in Dr. Bashford's judgment, especially important in determining our conception of the etiology of cancer.

Dr. Bashford draws the conclusion that the greater frequency of cancer in later life is not due to increasing suitability for the growth of cancer; on the contrary, animals become less suitable for this growth the older they are. He tells us that, practically, every mouse can be successfully inoculated if the experimental conditions are favourable.

Finally, Dr. Bashford tells us that mice can be protected against successful inoculation by preceding inoculation of cancerous tissue from another mouse, but not from an

animal of another species. But the fact to which Dr. Bashford attaches supreme importance, and which I confess surprised me greatly, was this: that an equally high degree of protection can be conferred by the inoculation, not of cancerous, but of perfectly normal, tissue—healthy blood, in fact—from one healthy animal into the body of another of the same species. I am sure that we shall agree with Dr. Bashford that this one fact, which seems to me of startling importance, is, as he describes it, “pregnant with future possibilities.”

I am sure we shall all agree as to the great importance of Dr. Bashford's paper.

DR. PAYNE: First of all, Mr. President, I must say how very much I am interested in Dr. Bashford's paper, and how greatly we are indebted to him for it.

I should like, if I may, to take up one or two points which seem to me of some importance.

The first point is the connection Dr. Bashford has established between cancerous growth and senescence, not only in man—of course it has been empirically known for a long time in man—but also in the lower animals . . . I agree, Sir, with the remark you made, that it is startling to find that young animals are as susceptible to receiving these noxious growths as older animals. This is not what one would expect. I suppose it will be explained in some way eventually, but at present it is somewhat difficult to reconcile it with other facts.

Dr. Bashford has this evening dwelt more upon points which have not been touched upon when this matter has been dealt with elsewhere; and, therefore, while we should be extremely glad to hear more about his personal contributions to the subject, we are glad to find that these other points are noticed.

He has made some interesting remarks as to the geographical distribution of cancer. Of course, it is very likely indeed that exaggerated views have been held upon that point; and it is also very likely that the enormous differences which at first sight appear are not found upon closer examination of all the factors. Again, as regards cancer among civilised nations, in an enormous country like India, where only a fraction of disease ever comes within medical purview at all, it is impossible to rely upon any figures which can be compiled.

Dr. Bashford has claimed for our own Registrar-General's department the first place for accuracy and precision, and

an intelligent consideration of all the factors bearing on the subject of registration of death and birth. He has also spoken in a not very complimentary manner as regards the statistics of Ireland. I wish it had been possible for him to say something about the statistics of Scotland; because, if I may say so, the Scottish returns are not nearly so good as those of England and Wales. I am always wondering how it is that such a great centre of intelligence as the Scottish capital has gone on for so many years with such very imperfect Registrar-General's returns: for such they are when compared with those of the English Office, which are founded upon the method established by Dr. Farr. The Scottish returns give us very little information on many points. With regard to the accuracy of diagnosis, I feel bound to make one statement in favour of Ireland. Dr. Grimshaw, who was Registrar-General for Ireland for a very long time, used to boast that his results were much more accurate than those of the English Office, and for this reason: that the Registrars in Ireland were all medical men, who took care, by questioning and so on, to get accurate returns of death. That was Dr. Grimshaw's position, and I am not able to criticise it. However that may be, it is very likely that the general level of medical practice in Ireland, not being so well paid, is not so high as in England; but I do not see that the statistics are capable of such very great errors as are attributed to them by Dr. Bashford.

As regards other European countries, their returns are certainly not as good as those of England. One cannot help thinking, however, that in a country like Germany, if they once recognise the great importance of proper registration, they will be able to carry it out in a very thorough fashion, because in Germany every person is known to the authorities. They know his age, where he lives, and all about him. I am convinced that if they once realised the value and importance of these returns, they could carry them out much more thoroughly than we can. And the same observation might be made with regard to Japan.

I do not know exactly why Dr. Bashford has entirely excluded the returns of Australia and New Zealand. I have not been in those countries, but I know many doctors there very well, and I believe their level of general medical practice is not at all low. There are good medical men there, most of them educated in London, although a fair proportion of them are now educated in their own country. I cannot see why their returns should not be accurate. And

if you read the reports, *e.g.*, of Victoria, New South Wales, and New Zealand, you will find that they are compiled with very great care, and that all such factors as age distribution (the distribution of age and population is not the same there as here) and sex distribution have been taken into account. The current return shows that in Victoria the mortality from cancer at certain ages was higher in the male than in the female sex, a state of things which is quite unknown in any European country, and which is explained by the fact that at these higher ages there are more men living than women in these places. The great care with which these exceptions have been stated is an indication of the care with which the returns have been prepared, and I cannot understand why Dr. Bashford has excluded them as untrustworthy.

With regard to another point, we know that in England and Wales, and also in Scotland (in Scotland the topographical reports are exceedingly minute), there are great differences in the registered mortality from cancer in different parts of the country. It was seen some time ago that these figures were not altogether satisfactory, because they did not take into account the age distribution in the several counties, but that point has been most carefully corrected by Dr. Tatham in all the recent reports. And what is the result? The result has been that the distribution of mortality from cancer has been changed. The same counties which formerly showed a high mortality from cancer in proportion to the death-rate now show a low mortality from cancer in proportion to the death-rate. . . . But remarkable inequalities still occur in different parts of the country, and I do not see that we can carry that any further. We must recognise that there are, in different parts of the country, many variations in the death-rate from cancer. And if so, why should not that be the case all over Europe? Why should we assume that, if we only carried out our registration returns with sufficient accuracy and investigated them closely enough, all differences would disappear and equality would result? If that were the case, cancer would be quite unlike any other disease; indeed, such a disease, unaffected by changes of time and space, is without a parallel. Therefore it does not seem probable (unless it should turn out that cancer is not in a certain sense a disease at all, but something in an entirely different category) that any such equality would be discovered.

I am exceedingly interested in cancer in early life. It

has been observed for a long time that the first few years of life give a much higher rate of mortality from cancer than the next five-yearly period. That appeared in statistics of England and Wales as long ago as 1851. In the statistics of age distribution of cancer for the period 1851-1860 it was found that the first year of life gave a higher rate of mortality than the next two five-yearly periods. I always thought that carcinoma was comparatively common in infants. I believe that if the figures for the first five years were further analysed, you would find that the great mass of cases come in the first two years, because that is the age when we find infantile sarcoma. From the Table on page 22, it appears that the difference between the distribution of cancer in the first two five-yearly periods of life is more than 8 per cent. in males and more than 6 per cent. in females. Now, if the kidney cases are taken away, the difference between the first five years and the second five years disappears. Now, malignant tumour of the kidney, although frequent in infants, is not frequent in later life, indeed it is very rare; it is a peculiar form of infantile growth. I must confess that the probable inference seems to me to be that these growths, which swell the figures for the period of infancy, are really congenital, or as good as congenital. It may easily happen that a tumour in the kidney in an infant will not be perceived until it is very large. I should think it probable that these tumours are, if not congenital, at least very nearly so, and therefore it seems doubtful whether they have any precise bearing on the question of cancer in general. The explanation of these kidney tumours has never appeared, I think.

Then there is the question whether sarcoma is to be regarded as cancer. It is true that sarcoma and cancer are always mixed up, and that some tumours of that kind appear to be related to the dissolution of certain portions of tissue in embryonic life. They are a very peculiar class of tumours altogether.

Well, now, with regard to the general results of Dr. Bashford's investigations in the London Hospital, they are most important and valuable, and I wish we had them rather more in detail. But I think it is clear that these figures cannot be compared with the statistics of death from cancer, as published. It must be remembered that these hospital figures represent cases of cancer, not necessarily deaths, and that the Registrar-General's statistics are compiled for entirely different purposes, and

include only those cases in which cancer is the cause of death. We do not know the number of cases which occur in the general population. Then, again, I think Dr. Bashford does not recognise sufficiently that the Registrar-General's certificates with regard to parts of the body do not state the primary seat of the disease; they do not profess to do so. The fact is that the death certificate is given to show what the patient died of. One example which will show the enormous difference is this: If you take the hospital statistics you find that cancer of the liver is hardly known. On the other hand, if you take the statistics of death-rate from cancer, you will find (I am taking the latest figures available) that in the last three years there were recorded 4190 deaths in males and 6935 deaths in females from cancer of the liver. In most of these cases the practitioner is probably perfectly right in saying that the patient died of secondary cancer. Another point connected with these two sets of figures is the distinction between accessible and inaccessible cancer. Accessible cancers are accessible to operations; and we know that owing to the enormous growth of surgery there are about ten times as many operations now as there were formerly, and that no cancer which is visible to the naked eye has much chance of escaping operation. As to cancer of the skin, I think we may hope that before long it will be a great rarity. Personally, I should think myself very much to blame if I allowed a patient to die of cancer of the skin. Then, again, cancer of the breast leads to the breast being so completely exterminated that the one disease of which that patient is perfectly certain not to die is cancer of that breast, because there is no breast left there. Every organ that can be removed by operation is removed, and cancer in that organ is removed from the category of "primary" cancer. The number of operations that can be performed is increasing every year. Every year surgery is mowing down primary accessible cancers and preventing them from being regarded as causes of death.

There is one other point, and that is, I am sorry to find that the name of Dr. William Ogle has not been included amongst those who have been distinguished in this work. In 1884 Dr. William Ogle remarked on the supposed increase of cancer. He himself did not believe that there was really an increase, but that the apparent increase was entirely due to improved diagnosis. He made the remark also that the increase of cancer was more marked in the male than in the female, because cancer in the female was

accessible, whereas the greater portion of cancer in males occurs in inaccessible parts of the body, *e.g.*, the abdominal organs; this, therefore, was the reason, he said, for the apparent increase being chiefly in the males. He took up the subject again in 1890, and he then made the first attempt to give a full account of cancer as affecting different parts of the body. He initiated a method, but he feared to give the full results. Afterwards, Dr. Tatham undertook the enormous task of publishing the statistics for cancer in all parts of the body. Dr. Ogle thought that this was perhaps too large a job, but he took what he called a sample of cases, and made what would be called in mathematics "first approximations." Nevertheless, the result is well worthy of attention, because you will find that these first approximations sketched out the final result; indeed, they anticipated the result which has been worked out in later reports, that is to say, the comparatively rapid increase of cancer in internal organs and its comparatively slow increase in those that are accessible to operation. Dr. William Ogle's results were recognised and stated by my friend Dr. Newsholme, but since that time they seem to have dropped out; I think, therefore, it is fair to say that, however well these things have been carried out by others, the origination of this idea, *i.e.*, the importance of observing whether cancer was accessible or inaccessible, and the bearing of that fact upon diagnosis as well as upon statistical results, was entirely due to Dr. Ogle.

Personally, I am very much indebted to Dr. Bashford for his most interesting paper.

SIR SHIRLEY MURPHY: I should like to join in the expressions of thanks which have been conveyed to Dr. Bashford for his able and interesting paper.

One point that interested me was whether Dr. Bashford's investigations were throwing any light upon the question whether improved medical knowledge would tend to increase the record of deaths from cancer or reduce them. One knows that error can creep in in two ways; but there will be, as it were, a fictitious loss in regard to the cases not diagnosed and which were really cancer, and a fictitious gain as to those wrongly diagnosed as cancer. I think Dr. Bashford's paper, and especially the Table relating to the London hospitals, shows that with improved knowledge there will be a great tendency for the figures to increase; that is to say, that looking at the accessible and inaccessible and intermediate cases of cancer in these

Tables, one sees that the proportion of total accessible cases is as 100 to 67, whilst the proportion of total inaccessible to wrongly diagnosed is as 100 to 6. Inasmuch as improved medical knowledge would tend to put the inaccessible on a level with the accessible, it would tend to increase the amount of cancer and would tend to increase the number of deaths from cancer.

Dr. Bashford has insisted very much on the need of investigating the amount of cancer in specified areas. I may point out that in considering the amount of cancer in well-to-do London districts and poor London districts, when correction is made for sex and age, one finds that the incidence of cancer for rich and poor is very much the same.

There is only one other small point. Dr. Bashford spoke about the comparison between a series of figures for the West and a series of figures for the East; but he has not mentioned one series which to my mind is the most interesting laboratory of statistics on the subject of the pathology of deaths in the East. It is very likely that he has taken account of it, but on the chance that perhaps he has not done so, I would like to draw attention to the very excellent statistics that are constantly being produced in the laboratory at Hong Kong. If Dr. Bashford has already come into touch with them, perhaps he would say whether anything definite has been brought out on that subject. You have there the peculiar fact of a limited population living under a law by which every death not certified by a European has to be examined in the laboratory, and there are in that way two thousand bacteriological and pathological examinations in the course of a year. This state of things is, I believe, unique, and it would be interesting to know what is the death-rate in that very typical Oriental population from this particular cause as compared with a European population. The statistics are admirably condensed by Dr. Horne, who was one of Dr. Bullock's students at the London Hospital.

DR. NEWSHOLME: I am sure we are all greatly indebted to Dr. Bashford for his very important paper. We all knew that Dr. Bashford was an extremely competent pathologist, but we did not know that he was equally competent in another capacity, namely, in that of a statistician.

One is bound to agree with the limitations that he has made so far as the application of statistical methods to the

discovery of the cause of cancer is concerned, though possibly he may have a little overstated those limitations. But I think we should remember the fact that by means of the statistics which he and his colleagues have initiated, we are able to say now, in the first place, that civilisation is not an essential factor in the causation of cancer. We are able to say again that we get cancer in fish and in the lower animals, and that the incidence of the disease in cattle and mice, for example, is practically in the same proportion as in man. Those are extremely valuable results to have been obtained from statistics, because they indicate that civilisation is not a main factor, and also that a meat diet is not necessarily an essential factor, since you get cancer occurring amongst animals like cattle, which eat no flesh, and also amongst races like Hindoos, who live chiefly upon rice. As a matter of fact, therefore, statistics have borne a rather important part in the results that, up to the present time, have been achieved; and though perhaps pathology will bear a still more important part, we must not allow statistics to be entirely set aside. Then, again, the fact that statistics have shown that cancer appears to be a disease of senescence is a very important result; and one of the most interesting results of the Cancer Research Fund so far has been the extension of the idea of senescence, not only to the whole being, but also to the particular tissues and organs of the body. The extreme instance given by Dr. Bashford of chorion epithelioma is a very striking instance indeed. I think, therefore, it may be said that if statistics have so far borne the greater part in that investigation of cancer, it is because of the failures of pathology.

With regard to the question of cancer houses, though undoubtedly the results do appear sporadic in the accounts given in medical journals with regard to cancer houses, the accounts given also indicate a presupposition as to the pathology of the disease, viz., that it is infectious. The writers of these accounts undoubtedly forget that they are dealing with very small figures, and that there may be a run of coincidences. They forget how long the arm of coincidences may be—how, for instance, if you set a sufficient number of persons tossing halfpence you will eventually get a man who will toss 1000 heads without a break. When one remembers coincidences like that, one is able to attach very little importance to numbers of cases in particular houses. . . . If those cases occurred alongside of our pathological knowledge that cancer was an

infectious disease, they would have much more importance.

As to the amount of cancer and the question of the increase of cancer, this is, I believe, a question of how the doctors enter the certificates. They may enter the certificate properly, and they may not. A doctor will enter a death, say, as due to abdominal tumour, and the certificate is sent to the Registrar-General. The President then writes to him and asks what was the nature of the tumour. The doctor then comes to the conclusion that it may have been a cancer, and he sends a letter to say that it was a cancer, and that death gets entered as cancer. But, after all, this is only a guess on the part of the doctor, and the positive guess may be as wrong in its definiteness as the original indefinite certificate was. Indeed, the original indefinite certificate may have been more trustworthy than the ultimate more definite statement. I am not saying that in any spirit of obstruction to the system of letter writing from the Registrar-General's office. I think it is a good system, and I am sure we all appreciate it; but in the process of education of the medical profession which is going on, the comparability of medical certificates is being destroyed, so far as these certificates are concerned, and we have to do with certification on different lines to what it was before.

I venture to differ from Dr. Bashford on one point, which I do not think he can really have considered fully. Cancer is not a rare disease; it is a very common disease indeed. It is much more common than typhoid fever, and nearly as common as pulmonary tuberculosis.

With regard to the Irish figures, I agree with Dr. Bashford's failure to believe in their trustworthiness. This fact was brought out some years ago with some clearness by a paper written by Mr. King and myself. One factor which was brought out in that paper was that the population of Ireland was an older population than that of England, although the percentage of average age had become lower in the last two consecutive decades. Another reason is, that owing to the smaller number of deaths in hospitals, there are fewer investigations of the cause of death. On the whole, then, I think one must reject the Irish figures as comparatively untrustworthy.

I should like to express my gratitude to Dr. Bashford for his admirable paper, and for the very suggestive lines of work which he has undertaken.

DR. F. W. ANDREWES: I am afraid I have nothing to add to the discussion as regards statistics of cancer, but I should like to coincide fully with what Dr. Payne has said as to the incidence of cancer during the first quinquennial period of life. Probably a large number of these cases are sarcomatous.

DR. DAWSON WILLIAMS: I did not intend to speak; but as you are kind enough to ask me, I would like to make one point, and that is, to take this opportunity of emphasising what Dr. Payne has said. I believe that unless a sharp distinction is made between these things that we call sarcoma that occur in infancy and the remainder, a considerable mistake will be made; and it occurs to one that by comparing the character of these sarcomas, their pathological characters generally, with those of cancer in later life, something might be learned. The question which arises with regard to this is, whether obsolescence and senescence are exactly the same things, and whether obsolescence is not a period of growth: all through foetal development there is this process of obsolescence constantly going on. Therefore, if we confuse obsolescence with senescence, we may be going wrong in that.

There is one obsolescent organ which has a chance of proceeding to senescence, and that is, the vermiform appendix, but I do not think it is the primary seat of cancer.

I should like to ask, if senescence is very important, why is it that cancer of the stomach and intestines is not very uncommon in middle life and in advanced life, because it is a common observation that when a man loses every other passion, he retains the desire to eat and the power of digesting his food.

DR. BASHFORD: Mr. President and Gentlemen,—In the first place I should like to thank you very much for the sympathetic manner in which you have listened to my somewhat scattered remarks.

It was, I think, quite impossible for me to refer to the statistics of Australia, of Hong Kong, and of other places. I am very familiar with Mr. Cook's valuable statistics for Victoria; but, as they did not seem to me to bring out any point which the statistics of Europe did not bring out equally well, I left them alone.

I have listened to Dr. Payne's remarks with great pleasure, more particularly because he was somewhat critical. I do not think it would be wise for me to reply to

him in detail, because whatever material I have excluded has been excluded because I did not think it was of sufficient importance.

There is one point to which I should like to refer. I do not wish to imply that I have been deliberately depreciating the quality of the statistics compiled in Prussia as compared with those in England. But when comparing different decennia the development and increased accuracy of Prussian statistics in recent years must be remembered. The fact that the number of cases of cancer recorded has absolutely increased, is a matter of great importance; but it is not very long ago that many Prussian towns introduced certification of the cause of death by medical men. I was only instancing Prussia as conveniently comparable, by reason of the state of things there, with a country like Ireland.

I think it is very probable that Dr. Payne, Dr. Andrewes, and myself are all in entire agreement as to cancer in children, viz., that these tumours are of a complicated structure, and that the growths on the kidney, etc., already referred to, are probably sarcomatous.

With regard to the question of separation of sarcoma and carcinoma, to which several speakers have referred, it is a very difficult matter to separate them. Clinically, they are one and the same thing. The medical man guesses at sarcoma just as he guesses at carcinoma. . . . For registration purposes they are the same thing. In hospital, at any rate, sarcoma, although relatively more frequent at birth and in early years than carcinoma, presents exactly the same phenomena as cancer. Dr. Murray and myself attempted to find out whether the same thing applied to the general population. We took selected areas and worked out the death-rate, and we found that for the general population the sarcoma increases with increasing years in exactly the same proportion as carcinoma.

I am very much indebted to Dr. Payne for drawing my attention to Dr. Ogle's work on the relation between accessible and inaccessible cancer, of which work I had a vague knowledge.

Then, in regard to Hong Kong, I am aware of the figures which are supplied there; I have been able to obtain them through the Colonial Office. But, unfortunately, cancer figures only to a very small extent in these returns, so far as they have come to my hands. The patients appear to be to a large extent young people, and the cases seem to be investigated more from a bacteriological point of view

(with special reference to plague, and so on) than with reference to the occurrence of the particular conditions. So far as the returns go which I have received from Hong Kong (I have not received the figures for this year), there was nothing very striking in their figures. The mere fact that there was nothing anomalous was probably the reason why they did not make any more impression upon my mind.

I should like to thank you for the attention which you have given to my paper, and the interest you have shown in this work. I should like also to remind you of the fact that this work can hardly be regarded as my personal work. I have had associated with me not only Dr. Murray, but also Dr. Cramer and Mr. Bowen. We are all associated with the Imperial Cancer Research; we are the servants of a corporation which enjoys opportunities such as have never yet been enjoyed by any group of persons engaged in the investigation of cancer; and if we have been able to advance the knowledge of cancer in any way, it is because it has been found possible to organise the inquiry upon a scale not hitherto attempted.

I think the profession as a whole should give due credit to the Royal Colleges of Physicians and Surgeons for the meritorious method in which they have set about instituting this inquiry.
